## SUPPORT FOR THE AMENDMENTS

Claims 1-3, 5, 6, 9, 10, and 12 were previously canceled.

Claims 23 and 24 are canceled herein.

Claims 4, 11, and 20 have been amended.

The amendment of Claims 4, 11, and 20 is supported by original Claims 1, 4, 11, and 12, as well as the specification as originally filed, for example, at page 3, line 23 to page 5, line 10 and page 6, line 6 to page 11, line 8 (in particular page 10, lines 2-11).

No new matter has been added by the present amendment.

REMARKS

Claims 4, 7, 8, 11, 13-22, and 25-32 are pending in the present application.

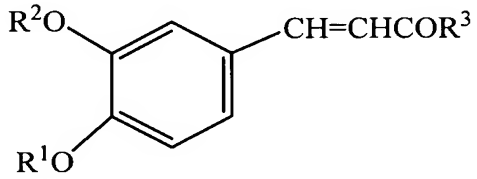
The objection to Claims 4, 7-8, 11, and 13-19 under 37 CFR §1.75 as being a substantial duplicate of Claims 20-31 is obviated in part by amendment and traversed in part.

In the Office Action, the Examiner objects to Claims 4, 7-8, 11, and 13-19 as being substantial duplicates of Claims 20-31. Applicants disagree with the Examiner and submit that Claim 4 and 20 are of *different* scopes. Specifically, in the proviso where $R^3$ is a hydroxyl group the definition of $R^1$ and $R^2$ differs in that Claim 4 permits for the possibility of an alkyl group, while the alkyl group is absent from the definition of $R^1$ and $R^2$ in Claim 20. As Claim 23 does not rely upon the situation where $R^3$ is a hydroxyl group, this claim has been canceled to avoid duplication of the scope of Claim 11.

Withdrawal of this ground of objection is requested.

The rejections of: (a) Claims 4, 7, 11, 14, 16, 17, 19, 20, 21, 23, 24, 26, 28, 29, and 31 under 35 U.S.C. §102(b) over Monache et al and (b) Claims 13, 15, 18, 25, 27, and 30 under 35 U.S.C. §103(a) over Monache et al, are obviated in part by amendment and traversed in part.

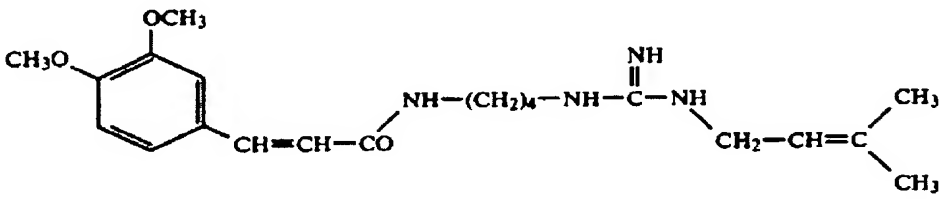
The presently claimed invention provides, *inter alia*, a method for treating hypertension, which comprises administering to a patient in need thereof an effective amount of a composition comprising a compound of formula (1):




(1)

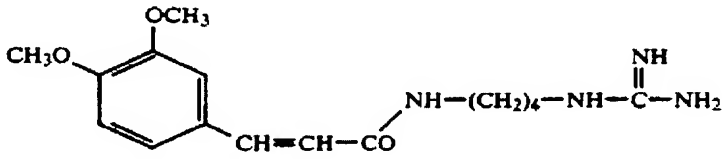
wherein, $R^3$ represents a hydroxyl group, or an *amino acid residue* selected from the group consisting of glycine, alanine, valine, leucine, isoleucine, phenylalanine, proline, serine, threonine, cysteine, cystine, methionine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine and histidine (see Claims 4 and 20, definition of $R^1$ and $R^2$, as well as the proviso have been omitted).

In the outstanding Office Action, the Examiner has rejected the claims as being anticipated and/or obvious in view of Monache et al. In making this rejection, the Examiner references the following compounds:




(3)

and




(5)

The Examiner contends:

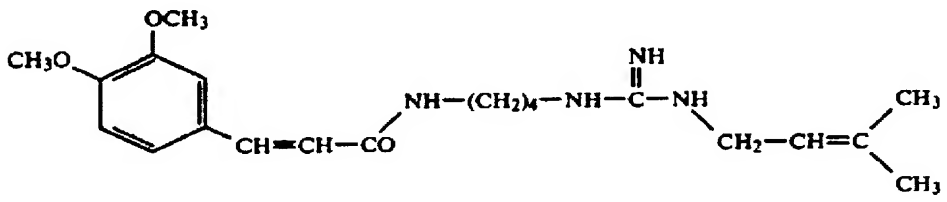
> "the term "amide bond residue derived from..." or "amide bond residue..." as recited in claims 4, 11, 20, 23, and 24 is construed to be amide bond containing any amino acid or amino acid derivative or residue selected from the group consisting of "glycine, alanine, valine, leucine, isoleucine, phenylalanine..." Thus, the examiner determines that the referenced compound containing arginine or arginine derivative at R3 position "metes and bounds" of the applicant's term "amide bond residue derived from..." or "amide bond residue."

To avoid misinterpretation of the claims, particularly with respect to the term "derived" and to clearly define the scope of the claimed invention, Applicants have replaced the phrase "an amide bond derived from a water soluble amino acid" with "an amino acid

residue" in Claims 4 and 11 and have replaced the phrase "an amide bond residue" with "an amino acid residue" in Claim 20.

In view of this amendment, it is clear that $R^3$ only represents a hydroxyl group or an amino acid residue, including arginine. Applicants remind the Examiner that amino acids have the general structure $H_2N$—CHR—COOH. Thus, the claims of the present application *require* the presence of the carboxyl moiety represented by —COOH.

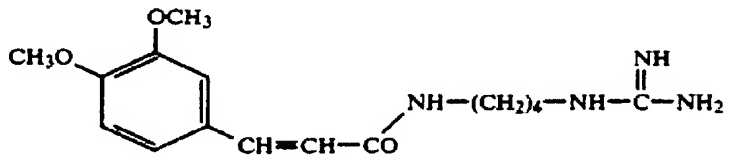
With respect to the compound (3) in Monache et al:




(3)

The Examiner apparently is of the opinion that this compound, which includes a prenyl group bound to the guanidine group, meets the previous claims by virtue of a broad interpretation of "derived". Applicants submit that the "derived" has been removed from the claims and, as such, compound (3) does not fall within the scope of compounds in the claimed invention.

With respect to the compound (5) in Monache et al:




(5)

The Examiner is again reminded that the claimed invention requires that $R^3$ is either a hydroxyl group or an amino acid residue, including arginine. Compound (5) does not fall within the scope of compounds of the claimed invention as the position equivalent to $R^3$ in formula (5) is not a hydroxyl group or an amino acid. The Examiner alleges that this compound contains arginine; however, this is clearly not the case as the compound (5) does not have the required carboxyl group.

Since Monache et al does not disclose any compounds within the scope of formula (1), this reference clearly fails to anticipate the claimed invention.

Applicants further submit that Monache et al fail to provide any disclosure or suggestion of how compounds (3) or (5) may be or should be modified to arrive at the claimed compounds. To this end, Applicants direct the Examiner to *Takeda Chemical Industries Ltd. v. Alphapharm Pty. Ltd.*, 83 USPQ2d 1169 (Fed. Cir. 2007) in which the Court of Appeals for the Federal Circuit clearly state that in order to find a *prima facie* case of unpatentability, a showing that the "prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention" was also required (*Takeda* at 1174, citing *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992); *In re Dillon*, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1990); *In re Grabiak*, 769 F.2d 729, 226 USPQ 870 (Fed. Cir. 1985); *In re Lalu*, 747 F.2d 703, 223 USPQ 1257 (Fed. Cir. 1984)).

Moreover, as clearly stated by *Takeda* at 1174, the Court squarely addressed the test for *prima facie* obviousness enunciated by the Supreme Court in *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 [82 USPQ2d 1385](2007) in the context of chemical compounds:

> That test for *prima facie* obviousness for chemical compounds is consistent with the legal principles enunciated in *KSR*.[2] While the *KSR* Court rejected a rigid application of the teaching, suggestion, or motivation("TSM") test in an obviousness inquiry, the Court acknowledged the importance of identifying "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does" in an obviousness determination. *KSR*, 127 S. Ct. at 1731. Moreover, the Court indicated that there is "no necessary inconsistency between the idea underlying the TSM test and the *Graham* analysis." *Id.* As long as the test is not applied as a "rigid and mandatory" formula, that test can provide "helpful insight"to an obviousness inquiry. *Id.* Thus, ***in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound.*** (*emphasis added*)

In view of the foregoing, Applicants submit that the present invention is not obvious in view of Monache et al as this reference fails to provide the requisite reason that would have led a chemist to modify the compounds disclosed therein in the manner necessary to arrive at the claimed compounds. Thus, Monache et al fails to support even a *prima facie* case of obviousness.

Applicants request withdrawal of this ground of rejection. Acknowledgement to this effect is requested.

Applicants submit that the present application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

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